RAPID INFLUENZA TEST IN YOUNG FEBRILE INFANTS FOR THE IDENTIFICATION OF LOW-RISK PATIENTS

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Abstract: We included 381 febrile infants less than 3 months with a blood culture and a rapid influenza test done as part of study of fever. The prevalence of serious bacterial infections was significantly lower in patients in the positive rapid influenza test (RIT) group (3/113; 2.65%; 95% CI: 0–5.6) than in patients in the negative RIT group (47/268; 17.5%; 95% CI: 13–22.0). No patient with a positive RIT had a positive blood culture (vs. 8 in the negative RIT group, 2.98%, 95% CI: 0.9–5.0). The cerebrospinal fluid culture was positive in 5; all of them had a negative RIT. The use of RIT in the Emergency Department on previously well-appearing febrile young infants without a known source during influenza seasons can help to identify infants with a lower risk of developing serious bacterial infections. Routine blood culture may be no longer necessary in infants with a positive RIT.

Key Words: infant, fever, bacteremia, blood culture

Accepted for publication April 23, 2009.

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DOI: 10.1097/INF.0b013e3181ab603c

Serious bacterial infections (SBIs) occur in 7% to 15% of febrile infants under 3 months of age.1,2 Considerable debate and variation in practice still exists and no management scheme has been universally adopted.3–5 Many guidelines address the need to perform urinary infection, complete blood count, and blood culture (BC) in all infants under 3 months with fever without a known source (FWS).

Influenza viruses are respiratory pathogens commonly found in children. The nonspecific presentation of influenza infection makes it difficult to distinguish from febrile or respiratory illnesses caused by other organisms. To enhance the clinical care of individual patients, rapid diagnostic tests yielding results in less than 4 hours and can help as a guide in the clinical management of suspected influenza cases. Febrile infants with a confirmed viral infection are at lower risk for SBI.6 Some authors have reported that the introduction of rapid influenza tests (RIT) in the therapeutic protocols designed for children aged 3 to 36 months with FWS can significantly reduce the number of diagnostic tests, the use of antibiotics and the number of hospital admissions. However, and according to the knowledge available to date, the value of RIT used to identify low-risk young febrile infants has not been analyzed.7

The objective of this study was to assess whether the RIT can help to identify low-risk patients and the impact brought about by introducing RIT in the management protocol of previously healthy infants less than 3 months with fever and no signs of focal infection during influenza seasons.

PATIENTS AND METHODS

A multicenter prospective study was carried out for 5 consecutive influenza seasons (2003–2008) at 2 Spanish tertiary teaching hospitals (Cruces Hospital, Bilbao, Basque Country, and the Sant Joan de Deu Hospital, Barcelona, Catalonia) evaluating approximately 150,000 children per year in the emergency department (ED). The Cruces hospital carried out the study for 5 consecutive flu epidemics (since 2003) and the Sant Joan de Déu hospital did so for 3 (since 2005).

We included the infants under 3 months with FWS with a temperature ≥38°C with a BC and a RIT practiced as part of the study of their fever. Children taking antibiotics prior to coming to the ED were excluded.

RIT was performed in the ED whereas the rate of incidence of influenza remained above 100 per 100,000 inhabitants. The commercially available assay Directigen Flu A and B Test Kit (Becton Dickinson, San Agustín del Guadalix, Madrid, Spain) for the direct and qualitative detection of influenza A and B viral antigens was used in all influenza epidemics at Sant Joan de Deu and in the first 3 influenza epidemics in the case of Cruces. In the last 2 influenza epidemics, the Binax NOW Influenza A and B Test was used at Cruces. RIT was performed bedside by the emergency attending physician (Bilbao) after suitable training or by a laboratory technician (Barcelona), after the manufacturers’ instructions. There were no confirmatory viral cultures.

Data Collection. Data were extracted from our registries of infants less than 3 months with FWS.

An electronic log of ED visits was reviewed weekly by a pediatric emergency physician to ensure proper identification of all potentially eligible infants and to assess a capture rate for the study. Hospital databases were checked to determine whether there were any new emergency visits or admissions after the initial discharge. A follow-up telephone call was made to patients not admitted to the hospital up to 10 days after discharge.

Statistical Analysis. SPSS 15.0 for Windows (SPSS Inc, Chicago, IL) was used for all statistical calculations. Data are expressed as mean and standard deviation for quantitative variables or numbers and percentages for categorical variables. Continuous data were compared with the Student t test. Categorical data were examined using the χ² test or the Fisher exact test. Statistical significance was defined as P < 0.05. Prevalence rates were expressed as a percentage with their corresponding confidence intervals.

The study was approved by the Research Committee of both EDs.

RESULTS

During the study period, 520 infants under 3 months with FWS were admitted to the ED. Of these, 139 were excluded for not having undergone RIT, BC, or both (Figure 1). Finally, 381 infants were included (238 from Sant Joan de Déu and 143 from Cruces); 202 (53%) were male. The mean age was 48.8 ± 22.3 days and 86 (22.6%) were aged 28 days or less. Twenty-six (6.8%) presented with some underlying diseases. All children were well-appearing except for 8.6 patients with a negative RIT (4 diagnosed with SBI) and 2 with a positive RIT (no SBI).

General characteristics, analytical results, and complementary tests ordered are showed in the Table 1.

RIT was positive in 113 patients (29.7%). Patients with a positive RIT had significantly lower hospital admission rates (n = 54; 47.8%) than those patients with a negative RIT (n = 198; 73.9%) (P < 0.001). The rate of unscheduled revisits to the ED was similar in both groups.

The prevalence of SBI was significantly lower in patients in the positive RIT group (3/113; 2.65%; 95% CI: 0–5.6) than in patients in the negative RIT group (47/268; 17.5%; 95% CI: 13–22.0).

The Pediatric Infectious Disease Journal • Volume 28, Number 11, November 2009

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Urinary culture by sterile method was obtained in 301 patients. Thirty-four (11.3%) were diagnosed with UTI. The prevalence of UTI was lower in the positive RIT group (31/229: 13.5%, 95% CI: 9.1–17.9) than in the negative RIT group (31/229: 13.5%, 95% CI: 9.1–17.9).

One hundred ten patients (28.9%) had CSF cultured, 13 in the positive RIT group and 97 in the negative group. The CSF culture was positive in 5 patients with a negative RIT (2 S. agalactiae, 2 Listeria monocytogenes, and 1 N. meningitidis).

**DISCUSSION**

This study demonstrates the usefulness of RIT in the management of previously healthy well-appearing infants with FWS during the influenza epidemic season. As shown by our results, patients with positive RIT have a lower risk to have a positive blood or urine culture.

As stated by the American College of Emergency Physicians, SBI should be suspected in febrile infants less than 28 days of age. It has been recommended that all these patients be evaluated and admitted to the hospital. The committee, however, did not specifically address the issue of children 28 days to 3 months of age. In the editorial comment, and in a more recent review, Baraff recommended that these young infants be treated as outpatients should they meet clinical and laboratory low-risk criteria. Rochester and Philadelphia scoring systems are the most widely used low-risk criteria. None of these take RIT into account during influenza seasons.

In the present study, no positive influenza patients were reported to have a clinical diagnosis of bacteremia. According to the results of our study, it seems reasonable to include the RIT during the influenza season to identify infants at low risk for SBI; moreover, BC need not be routinely obtained in young febrile infants.

RIT was performed with the Directigen Flu A+B or Binax tests because of their high diagnostic accuracy, their ability to distinguish between both viruses and the experience obtained by applying this tool to young infants. Although viral cultures are the standard, they were not obtained in our patients because of their very limited usefulness in the ED. RIT, in the context of the influenza season or whenever there is a high degree of clinical suspicion, would be best used as a confirmatory test because the positive predictive value is greater than 95% and the number of false-positive cases is small. It is to be expected that laboratory tests and radiographs in any age group would increase length of stay in the ED, particularly during influenza periods when ED are overcrowded. It is very important to restrict the use of RIT to the influenza season when a significantly high number of false-positive tests is not expected.

This study has several limitations. Not all infants with FWS admitted during the flu epidemics were included, mainly because they had not undergone RIT or BC. In the follow-up, however, no SBI was diagnosed in patients with a positive RIT and no BC. Urine dipstick testing was performed in all patients, but urine was not cultured in all influenza positive infants under 3 months. All these patients did well in the follow-up, but it cannot be stated that all their urine cultures were negative. In our series, however, 4% of influenza positive infants presented positive urine culture. This emphasizes the necessity to get a urine culture in this population regardless the result of the RIT.

Our results confirm data obtained in the 2 previous studies carried out by our groups that looked into the impact of rapid influenza test on management of febrile infants less than 36 months without signs of focal infection.

We believe that the use of rapid testing for influenza in previously healthy well-appearing febrile young infants without a known source during influenza seasons in the ED can help to identify...
those infants at a lower risk to have a SBI. It is a test that can be performed easily and quickly at the bedside by the attending physician. The approach used for febrile infants with a positive RIT may be more conservative and routine BC may be no longer required if the infant has a good clinical appearance and a negative urine dipstick.

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